Chapter

Introductory Chapter: Osteoporosis Overview

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1. Introduction

Osteoporosis is a skeletal disease, characterized by a thinning of the bone (loss of bone mass), accompanied by a deterioration of its internal architecture that compromises its resistance, producing a greater fragility of the bones and an increased risk of fractures. The most affected bones are especially those of the spine and hip, although any bone in the body can be involved. As the main risk factor for suffering bone fragility fractures, which increases with age, it is an important public health problem that has undoubted social, health and economic repercussions; but above all it causes pain, functional limitation and severe alteration in people's quality of life.

The World Health Organization (WHO) defines it mainly in women as "the presence of a bone mineral density (BMD) less than or equal to 2.5 standard deviations below the average bone mass of healthy 20-year-olds", which is carried performed using a specific radiological test, called bone mineral densitometry. Since bone loss often occurs without symptoms, osteoporosis is often considered a "silent disease" that can occur in both sexes and increases with age. As bone tissue deteriorates, together with the architecture changes, the bone becomes so weak, that a relatively minor bump or fall, causes a vertebra to fracture or break. That is, the clinical manifestations of osteoporosis appear as a consequence of its complications, which are spontaneous fractures or after minimal trauma. Many environmental factors are involved in their onset [1].

However, there is a risk of considering that the loss of bone mass, causes only musculoskeletal pain. Women are more susceptible to suffering from bone fractures, as direct consequences of this disease, due to the fact that faced with a calcium deficiency in the diet, together with a vitamin D deficiency, during pregnancy and lactation, the body goes to diminish the reserves of calcium in the bone, which is the cause of gradual loss of bone mass. For this reason, its appearance is later and more frequently in amenorrheic or post-menopausal women, who also have a decrease in the production of estrogens by the ovaries and other hormonal deficiencies that affect metabolism in the bone. Factors that increase the risk of developing osteoporosis are calcium and vitamin D deficiencies due to malnutrition, sedentary life or lack of physical activity, and tobacco and/or alcohol consumption. Other secondary causes have been reported, such as celiac disease, monoclonal gammopathy of uncertain origin, chronic renal failure, diabetes mellitus, and renal tubular acidosis. Some epigenetic factors can be associated [2].

The best strategy for treating osteoporosis, is the prevention. Bone, or bone tissue, is a very dynamic living tissue throughout life, which is constantly formed (ossification), grows and remodels (bone turnover). For these processes (formation, growth and remodeling), important for the integrity or strength of the bone, hormonal activities, certain nutrients (calcium, phosphorus, magnesium,

vitamin D, vitamin K) and physical activity take part. Therefore, they are recognized as factors that play an important role in the prevention and treatment of osteoporosis. You have to get a good BMD and maintain it throughout your life. For this, it is necessary to achieve optimal bone formation in the youngest and then avoid loss of bone mass in adulthood and old age.

To achieve these goals, it is necessary to carry out a diet that provides the essential nutrients for the formation, growth and maintenance of bones. It is important to guarantee the consumption of the daily needs or minimum requirements of Calcium (1300 mg/day), Phosphorus (1250 mg/day), Magnesium (420 mg/day) and Vitamin D (20 mcg/day equivalent to 800 IU/day), through normal nutrition (daily consumption of foods that contain these nutrients) or supplementation. Perform appropriate physical exercise for each age through frequent outdoor activity, which ensures prudent sun exposure, for the synthesis of vitamin D in the skin, but avoiding overexposure, due to the risks it has on skin health [3–5].

2. Classification

Taking into account the causes that produce it, osteoporosis can be classified as primary and secondary.

2.1 Primary or involutive

It is the most common type of osteoporosis. This diagnosis is established after evaluating the patient, when the cause/s that can be related, are not found. In turn, primary osteoporosis can in turn be subdivided into juvenile, postmenopausal, age-related, and idiopathic forms.

2.2 Secondary osteoporosis

When the loss of bone mass is caused by another disease, or by the use of particular drugs. Fractures occur most frequently at the level of the hip bones, vertebrae of the spine, and wrist. Vertebral fractures can cause loss of height of the spine as a whole and deformity of the rib cage.

Depending on the results obtained in BMD, the results can be classified according to the T scale, which refers to the mean bone density of the healthy population of the same sex and 20 years of age in the following categories:

2.3 Normal

When bone mineral density is greater than −1 standard deviation (SD) on the T scale.

2.4 Osteopenia

When the BMD presents a standard deviation between 0 to −1, on the T scale. This variety is not included in osteoporosis and generally does not require drug treatment.

2.5 Osteoporosis

If bone mineral density is less than −2.5 standard deviations on the T scale.

2.6 Established osteoporosis

When there is osteoporosis and it has caused a fracture [6, 7].

3. Epidemiology

Osteoporosis and its related complications, are one of the main health problems in the world. This disease is estimated to affect at least to 200 million of women globally and is a major cause of morbidity and mortality. Among North American postmenopausal white women, 57% are osteopenic and 30% osteoporotic, and from the age of 80 ahead, 27% of women present osteopenia and 70% osteoporosis, with a large increase in the latter.

It is reported that approximately 40% of white US women and 13% of white US men in their 50s will experience at least one brittle bone fracture in their lifetime. It is also estimated that 1 in 3 women and 1 in 12 men over the age of 50 suffer from osteoporosis. And it is responsible for millions of fractures annually, many of which include the lumbar vertebrae [8, 9].

4. Etiology

The bones of the body are subjected to continuous remodeling through processes of formation and reabsorption, they also serve as the body's calcium reservoir. From the age of 35, the loss of bone mass begins. Multiple diseases or sedentary lifestyles, can increase the bone loss causing osteoporosis at an earlier age.

The main mechanisms that cause osteoporosis are: 1/. Lack of sufficient bone mass, during the growth process. 2/. Excessive bone resorption mediated by osteoclasts. 3/. Inadequated new bone formation by osteoblasts, during the continuous process of bone renewal.

Menopause is the main cause of osteoporosis in women, due to the decrease in the production of estrogen hormones, which are reduced by physiological menopause or by surgical removal of the ovaries, causing rapid bone loss. Women, especially Caucasian and Asian, have lower bone mass than men. Bone loss results in decreased bone strength, easily leading to wrist, spine, and hip fractures.

However, there are a considerable number of causes of osteoporosis at any age that are not usually recognized or valued, but that can be identified if the patient undergoes an appropriated evaluation. Among them, the most common are undiagnosed Celiac Disease, due to the fact that it occurs frequently in a subclinical or asymptomatic way, and in people with negative antibody tests, untreated Non-Celiac Gluten Sensitivity, Monoclonal Gammapathy of uncertain significance, patients with Chronic Renal Failure, Diabetes Mellitus, and with Renal Tubular Acidosis.

In people with Celiac Disease or Non-Celiac Gluten Sensitivity without diagnosing, or following a gluten-free diet, the causes of both osteoporosis and osteopenia, are not limited to the existence of possible nutritional deficiencies, but may be due to processes inflammatory or autoimmune diseases in which the consumption of gluten can cause the development of autoantibodies.

The causes of secondary osteoporosis can be divided into several groups: endocrinological, gastrointestinal, by drugs, the presence of prolonged amenorrhea, or by various malignant tumor processes.

4.1 Endocrinological

Hyperthyroidism Hyperparathyroidism, Cushing's Syndrome, Type 1 Diabetes (insulin-dependent), Addison's disease, Sarcoidosis, Hypogonadism, Gigantism.

4.2 Gastrointestinal

Celiac disease, Ulcerative Colitis, Crohn's disease, Liver disease (especially Primary Biliary Cholangitis), Gastrectomy and Intestinal resection.

4.3 Drugs

The most frequently implicated are corticosteroids, lithium salts and some anti-epileptics, among others.

4.4 Various processes

Prolonged malnutrition, Large intestinal resections, Chronic alcoholism, Rheumatoid arthritis, Prolonged immobilization, others [10].

5. Clinical symptoms

Osteoporosis usually does not cause any symptoms. For this reason, it has been called the "silent epidemic". However, the error of considering that the loss of bone mass causes musculoskeletal pain is widespread. and patients are frequently referred to a specialist for this reason with suspected osteoporosis, especially pre-menopausal women or in young people.

The main clinical manifestations of osteoporosis are due to its complications, such as fractures, which mainly occur in the spine, wrists and hips. They are caused by minor trauma, such as a simple fall. This is why they are called "brittle fractures." They are usually classified broadly as "vertebral" and "non-vertebral." They produce the same symptoms as other fractures in the same location and are characterized by the presence of pain, deformity and functional impotence.

Vertebral fractures are the most frequent. They appear as a result of an effort, when carrying weights or bending over, but they can also appear spontaneously, without finding an apparent reason. They are typically accompanied by acute pain, which increases with movement and decreases with rest. The intensity of the pain usually decreases after the first 2–3 weeks and disappears in some cases after more than two years.

However, about two-thirds of vertebral fractures do not cause symptoms and can only be verified by radiography of the thoracic or lumbar spine. In some patients, as a consequence of structural alterations of the spine, instability of the spine may develop which is accompanied by muscle contractures and ligament tension, which can cause chronic pain.

The most serious fractures are those of the hip, usually as a result of a fall. Although there is no data to confirm this, the popular belief has spread that as a result of significant osteoporosis, the patient fractures the hip while standing and then falls, although this is not always the case [11].

6. Diagnosis

Osteoporosis is diagnosed by the evaluation of the findings of bone mineral densitometry test, which measures the amount of bone mass in the skeleton.

Its measurement is usually carried out at the level of the central skeleton (lumbar spine and/or neck of the femur) using specific radiology equipment (dual-DXA radiological densitometry). In the event that the central skeleton cannot be measured due to the existence of advanced osteoarthritis, fractures or prostheses that would invalidate the result, densitometry can be performed in such cases on the forearm or heel with other equipment (peripheral measurement DXA or quantitative ultrasonometry).

To evaluate the possible secondary causes of osteoporosis, basic and complementary tests are carried out; the latter, depending on the clinical suspicion:

7. Basic tests

1/. Comprehensive, complete and detailed medical history. 2/. Complete blood count with count of the three series, leukocyte formula and sedimentation rate. 3/. Coagulation study, to see if it is normal, or is accompanied by some alterations. 4/. Complete Biochemistry study, including serum levels of calcium, phosphorus, creatinine, alkaline phosphatase, sodium, and potassium. 5/. Serum levels of TSH and vitamin D. 6/. Total protein and albumin levels, with associated proteinogram to detect possible presence of gammapathies [12].

8. Supplementary tests

a. Determination of serum levels of parathormone, bone-specific alkaline phosphatase, prolactin and immunoglobulins.

b. Quantification of IgA, IgG and IgM immunoglobulins.

c. Determination of celiac disease antibodies (anti-transglutaminase IgA)

d. Biochemical markers of bone remodeling, such as the C-terminal propeptide of type I procollagen.

e. Fasting serum T3, T4 and plasma cortisol levels.

f. 24-hour urine study, to quantify total calcium and phosphorus elimination in one total day

g. Gastroscopy with taking duodenal biopsies to study celiac disease

h. Determination of insulin growth factor type 1 (in cases of anorexia and diabetes)

i. Fibroblast growth factor 23 levels

j. Bone biopsies samples, only when considered necessary in special cases

9. Treatments

The first step before recommending a treatment is to evaluate the patient for determining if its case belongs to primary or secondary osteoporosis, in order to detect the diseases that cause it, some of which often go unnoticed. If the causative disease is adequately treated and low bone density for age persists, treatment will depend on the dynamics of the bones.

The general guidelines are based on recommending an adequate amount of calcium in the diet, the practice of physical exercise and the use of medications that contribute to the maintenance or increase of bone mass. The main drugs used are calcium salts alone or associated with vitamin D, bisphosphonates, strontium ranelate, raloxifene and teriparatide, denosumab, calcitonin and hormonal treatment with estrogens.

Bisphosphonates are the most widely used group of drugs. Within these drugs are alendronic acid (alendronate), risedronate and ibandronate.

10. Diet, calcium and vitamin D supplements

Calcium is necessary to support bone growth, bone repair, and for maintaining the bone strength and is one of the main pillars of osteoporosis treatment. Calcium intake recommendations vary depending on the country and age. For individuals at high risk of osteoporosis over the age of 50, the amount recommended by the US Health Agencies is 1,200 mg per day. Calcium supplements can be used to increase dietary intake, and their absorption is optimized by taking several small (500 mg or less) dosages throughout the day.

The role of calcium in preventing and treating osteoporosis is unclear because some populations with extremely low intakes of calcium have low rates of bone fracture, and others with a high intake of calcium through both milk and its derivatives have a lot of bone fracture.

Other factors, such as protein intake, salt, vitamin D, exercise, sun exposure, also influence bone mineralization, making calcium intake one of many factors in the development of osteoporosis. Some studies show that a large intake of vitamin D, reduces the risk of fractures. However, other researchers have not confirmed these conclusions, so this aspect of treatment is a matter of debate [13].

Vegan diets can cause significant nutritional deficiencies, including calcium and vitamin D. These people tend to have low bone mass. The European Prospective Study on Cancer and Nutrition (EPIC, published in 2007) concludes that vegans have a 30% higher risk of bone fractures, than meat, fish and other subtypes of vegetarians, probably due to their considerably lower average consumption of calcium, although those who consume adequate amounts of this mineral have the same risk of fracture as the general population.

The risks of nutritional deficiencies and serious health consequences are especially important during pregnancy, in babies and in children. These deficiencies can only be prevented by choosing fortified foods or taking regular dietary supplements, for which personalized education and evaluation by nutrition professionals is essential. Both parents and adolescents may lack the necessary knowledge for proper vegan diet planning.

11. Physical exercise

Multiple studies confirm that maintaining an ideal weight and periodical performing aerobic physical exercise or resistance exercises, can maintain or increase

bone density (DO) in postmenopausal women. Many researchers have evaluated which types of exercise are the most effective in improving BD and other measures of bone quality, however results vary [14].

One year of regular exercise increases bone density and proximal tibial moment of inertia in normal postmenopausal women. Walking, gymnastic training, stepping, jumping, endurance, and strength exercises result in a significant increase in bone densities from the second to fourth lumbar vertebrae in postmenopausal osteopenic women. Other benefits of physical exercise include improved balance and reduced risk of falls.

12. Bisphosphonates

In confirmed osteoporosis, this group of drugs belong to the first line of treatment and they are the most widely used and those with the most experience of use. The most commonly used are alendronic acid, 10 mg per day, or 70 mg per week, risedronic acid, 5 mg /day or 35 mg/week, ibrandonic acid 150 mg once a month, or zoldronic acid, 5 mg once a year intravenously.

Osteoporosis is caused by the decrease in the tissue that forms bone, both in the proteins that make up its matrix or structure and in the mineral salts of calcium it contains. As a consequence, the bone is less resistant and more fragile than normal [15].

Oral bisphosphonates have a relatively low absorption, and is recommended that food or liquids should not be ingested within 30 minutes of administration. They can cause side effects such as esophagitis and, rarely, jaw osteonecrosis. Zoledronic acid administered once a year intravenously does not present the problems of oral intolerance, but it frequently causes as a side- effect a picture of joint pain and fever that is not serious.

13. Teriparatide

It is an analog of human parathyroid hormone that is made up of a sequence of 34 amino acids, corresponding to the active fragment of the natural hormone. It is therefore a new bone-forming drug and is indicated in the treatment of osteoporosis.

It is used primarily in patients with established osteoporosis and a history of fractures, with particularly low bone mass, or with various risk factors for fractures. A daily injection of 20 micrograms is given subcutaneously. In some countries its use is only authorized if bisphosphonates have not been effective, or are contraindicated. Teriparatide is contraindicated in various circumstances, such as pregnancy, Paget's disease, hyperparathyroidism, and malignant tumors involving the bone [16].

14. Strontium Ranelate

It is an oral treatment alternative. It is effective in preventing vertebral fracture, but not hip fractures. It works by stimulating the proliferation of osteoblasts and also inhibits the proliferation of osteoclasts.

It is administered orally at a dose of 2 g daily. It does not have the side effects of bisphosphonates, as it does not cause gastric or esophageal symptoms. However, it has been shown to increase the risk of venous thromboembolism and can cause some serious dermatological reactions [17].

15. Hormone replacement therapy

15.1 Estrogens

Although it is known that estrogen treatment can be effective in stopping the loss of mineral content from bone in women after menopause, its administration as a treatment for osteoporosis is not currently recommended, due to the possibility of serious side effects and the existence of other safer alternatives. For this reason, estrogen therapy, as a hormonal treatment for menopause, is not recommended for the treatment of osteoporosis [18].

15.2 Testosterone

In men with testicular hypofunction, the administration of testosterone improves bone quantity and quality. However, there are no studies on its effects in reducing fractures or in men with normal testosterone levels [19].

15.3 Raloxifene

It is a selective estrogen receptor modulator. Drugs of this therapeutic group, bind to specific receptors on cells, simulating the activity of estrogens in certain tissues. Raloxifene acts on bone by decreasing osteoclast bone resorption and making vertebral fracture less likely. However, it is not effective in trying to reduce the incidence of hip fractures [20].

15.4 Denosumab

It is a drug that belongs to the group of biological agents, made up of monoclonal antibodies. In June 2010, its use was approved in the USA by the FDA to be used in the treatment of osteoporosis in post-menopausal women at high risk of fractures. Its mechanism of action is based on binding to a cellular receptor called RANKL, preventing its activation, which causes an inhibition in the formation of osteoclasts and their functionality. Osteoclasts are cells that are involved in the loss of bone mass and therefore favor the appearance of fractures [21, 22].

15.5 Prognosis

Patients with osteoporosis have an increased mortality rate, due to the greater likelihood of fractures occurring. The highest rate associated with osteoporosis is related to hip fractures, with an approximate mortality of 13.5% six months after they occur and 20–30% during the first year, which means that the risk of death, increases 2 to 10 times, higher than expected, in the population with similar characteristics. The causes of death are diverse and in many cases, they are not directly related to the presence of fractures.

The bad consequences of hip fractures are not limited to their hospital treatment, but to the deterioration of the quality of life, due to the residual disability that they entail. They can cause decreased mobility and the development of various complications, such as deep vein thrombosis, pulmonary embolism, and pneumonia.

At least 13% of the people who suffer them, need permanent help to be able to move. Vertebral fractures have less impact on mortality than hip fractures, but they can lead to thoracic and abdominal deformities, causing chronic pain that is difficult to control. Multiple vertebral fractures can lead to the appearance of significant

lordosis and kyphosis of the spine, with the consequent increase in pressure on internal organs, which can decrease the respiratory capacity of affected subjects [23, 24].

Osteoporotic fractures are generally associated with a significant decrease in health-related quality of life [25].

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